

Skeletal Muscle

Introduction

There are two main types of muscle: smooth and striated. Striated muscle can be broken down further into **cardiac**, **visceral**, and **skeletal** muscle. **Striations** are a phenomenon caused by the organization of the muscle fibers within a muscle—all the contractile units are arranged next to one another, oriented in the same direction, traveling from origin to insertion. The contractile units of smooth muscles are not lined up together in a plane, so they don't have striations. This lesson focuses on skeletal muscles.

Skeletal Muscle Function

A skeletal muscle contracts to bring two bones closer together in a straight line within one plane. The **origin site** is the attachment of muscle to the bone that moves the least, while the **insertion site** is the attachment to the bone that moves most. For example, the biceps muscle inserts on the forearm and originates at the humerus. When contracted, the shoulder and humerus generally stay in the same place, and the hand/forearm comes up to the humerus. Though an isolated muscle is really just bringing two points together, multiple muscles can work together to generate more complex movements around joints.

Each muscle is surrounded with connective tissue, which weaves into the muscle. At certain points, this tissue forms larger cords of fibrous elastic tissue—**tendons**—which connects muscle to bone. Tendons are fibrous, white, and thick. Muscle, for the most part, is beefy, striated, and red.

Embryology of Skeletal Muscle Cells

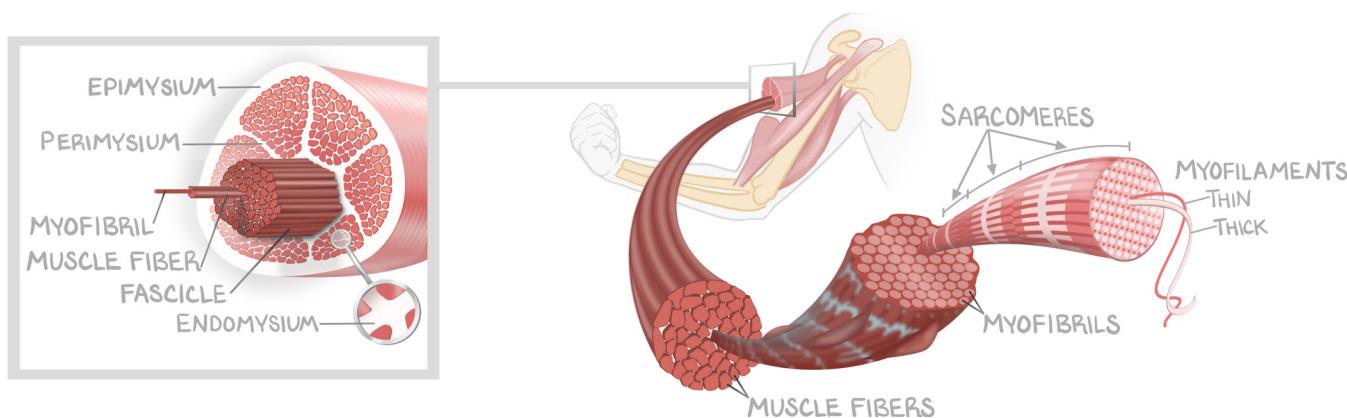
During embryologic development, myoblasts line up in single file, grab hold of the cell in front and in back, and merge. This “merging” (mechanism omitted purposefully) results in formation of a **single multinucleated cell**, the **muscle fiber**, which has continuous cytoplasm from origin to insertion. Muscle cells are **permanent** and fully **differentiated**—they can never be induced back into the cell cycle. This means that if a muscle is removed, becomes necrotic, or in any way loses fibers, it cannot be regenerated. Skeletal muscle can respond only with **hypertrophy** (increasing size against stress) or **atrophy** (decreasing in size because of lack of use).

Organization of Skeletal Muscle: From Bigger to Smaller

The muscle cell is called a muscle fiber. Skeletal muscle fibers are one cell wide and continuous from origin to insertion.

If you zoom out from the muscle fiber, you go toward “bigger.” Muscle fibers that are lined up side by side are known as a **bundle** or **fascicle**. A group of fascicles together make the “**muscle**”—the thing someone shows off in the gym. All the fibers within a fascicle are aligned next to each other and are heading in the same direction, from origin to insertion.

The connective tissue that surrounds the muscle carries the blood vessels and neurons and is named based on its relationship with the fibers. **Endomysium** surrounds individual muscle fibers, and so has the smallest nerve projections and blood vessels. **Perimysium** surrounds fascicles, with even larger vessels. **Epimysium** is the sheath of dense connective tissues that surrounds the muscle. Epimysium becomes the tendons of the muscle that connect to the bones. The major arteries and nerves penetrate the epimysium.

**Figure 11.1: Organization of Skeletal Muscle**

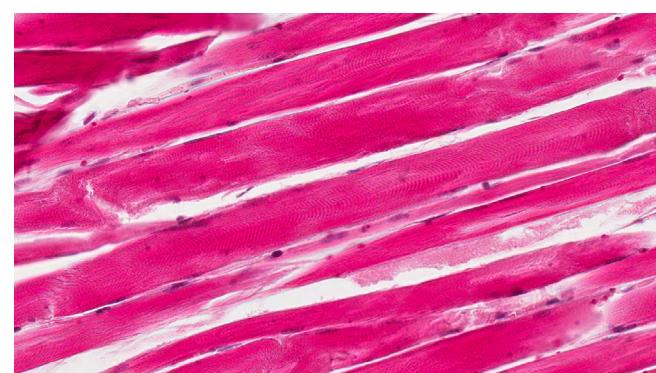
On the left we see the organization of fibers surrounded by endomysium, fascicles surrounded by perimysium, and muscles surrounded by epimysium. All muscle fibers are arranged in the same orientation, from origin to insertion, and all fibers are next to each other. On the right, we dive deeper into the organization of the muscle fibers. Muscle fibers are made of myofibrils, all lined up in the same orientation as the fibers, just inside the cell membrane. Myofibrils are made of repeating units called sarcomeres. Sarcomeres comprise repeating units of thin and thick myofilaments.

Back to our muscle fiber. Zooming in reveals that each fiber consists of even smaller units, called **myofibrils**, which are also longitudinally arrayed. They are separated from each other by a **sarcoplasmic reticulum**, longitudinally arrayed and running in the same direction as the fibrils. The sarcoplasmic reticulum is the muscle cells' version of the endoplasmic reticulum. The cell membrane of muscle cells, called the **sarcolemma**, surrounds the multiple strings of fibrils and sarcoplasmic reticula. To make room for these fibrils and reticula, **skeletal muscle nuclei** are always found on the edge of the cell, next to the cell membrane. There are other organelles, of course, such as mitochondria, but we're staying focused on the uniqueness of skeletal muscle fibers. Between fibers are connective tissue and capillaries.

Zooming in even more, to a single fibril, reveals that each fibril is made up of repeating units stacked on each other. This repeating unit along the length of the fibril is called a **sarcomere**. The sarcomeres of one fibril are actually oriented longitudinally with the sarcomeres of the neighboring fibril. They are also arranged such that sarcomeres begin and end at nearly the same point as the neighboring fibril's sarcomeres. Between fibrils are other intracellular organelles—nuclei, mitochondria, and endoplasmic reticulum.



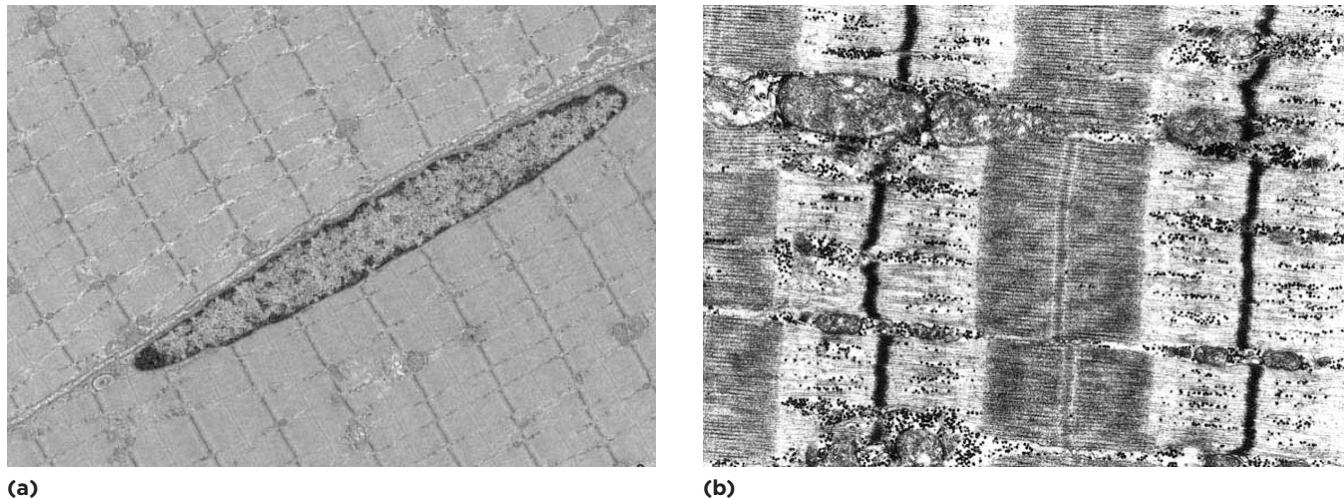
(a)



(b)

Figure 11.2: Light Microscopy of Skeletal Muscle: Looking at Multiple Fibers

(a) Note the longitudinal arrangement (all fibers running left to right on the page, in the same direction) as well as the many nuclei within each fiber, pushed off to the side. (b) Note the striations (the repeating pattern of A bands and I bands) and interfiber structures such as capillaries carried in the fibrous white connective tissue.



(a)

(b)

Figure 11.3: Electron Microscopy of Skeletal Muscle Fibers: Looking Inside Just One Fiber

(a) Zoomed-in electron microscopy showing two skeletal muscle fibers lined up next to each other and traveling in the same direction. Within each cell there are fibrils, long strings running next to each other. Within each fibril is a repeating pattern of the sarcomere, each end of the sarcomere approximately in line with the sarcomere of the neighboring fibril. The nucleus is seen on the edge of one of the cells. Most of the fiber is comprised of fibrils. (b) Zoomed-in electron microscopy of several sarcomeres. The intensely dark band is the Z line; the light band is actin. Then there is a dark grey (actin-myosin overlap), brief light band (myosin only), and finally the grey A band. The repeating pattern will be discussed in more detail next section.

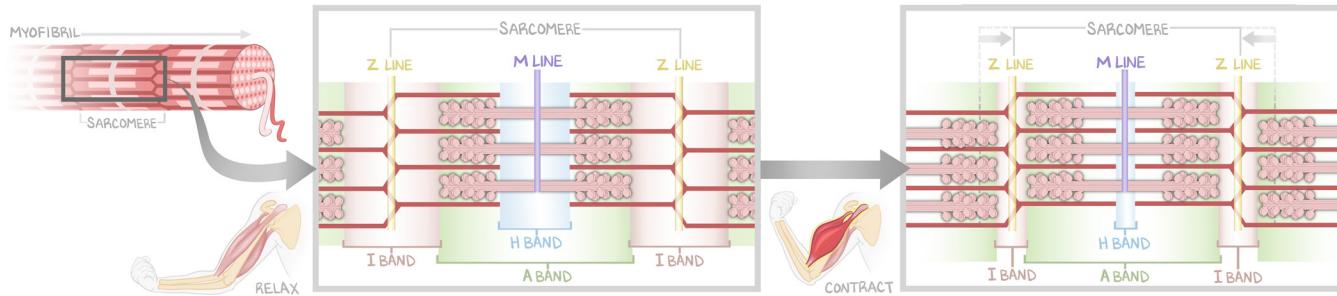
Fibers are lined up next to each other, traveling in the same direction. Fibrils within a fiber are also lined up next to each other, traveling in the same direction. Sarcomeres within fibrils are stacked on top of each other for the length of the fibril but also in perfect alignment with their neighbor fibril. So when a contraction is signaled, from fibril to muscle, every unit of contraction is contracting in one plane, together, at the same time.

Each fibril is made up of **myofilaments**. Myofilaments are **myosin 2** and **actin**. Together, these make up the contractile unit, the **sarcomere**. We'll go into a little physiology of myosin and actin once we cover the sarcomere. But, to understand the sarcomere, you first need to know that the filaments of myosin are many myosins stuck together so they are big and thick, and will **appear darker** than actin on an electron micrograph. Actin, the thin filament, **appears lighter** because it is so much thinner than myosin. Areas of overlap between myosin and actin appear **darkest of all**.

The Sarcomere

We need to get through A band, H band, I band, Z line, M line. This is confusing because the letters don't mean what students want them to mean, and many go crazy trying to memorize. We'll get into the details momentarily, but I want to start with a major realization that blew my mind when I was studying. You **cannot define the I band with one sarcomere**; it only makes sense if you have three sarcomeres next to each other (unless you already understand it, in which case, good for you). A sarcomere is defined Z-line-to-Z-line, and the I band crosses the Z line into the next sarcomere.

I start with the lines because I can associate their letters with something that "makes sense." The **M line** is in the **Middle** of the sarcomere, and has only **myosin** attached to it. The **Z line** is the end of a sarcomere, just as **Z** is the last letter of the alphabet. And since myosin is attached to the M line, and actin needs something to attach to, actin attaches to the Z line. The **lines make sense** this way with their naming.

**Figure 11.4: Sarcomere**

Artist's rendition of the sarcomere, demonstrating the M line, Z lines, A band, H band, and I bands. During contraction, within the sarcomere, the M line does not move, and the Z lines come closer to the M line. The A band does not change. The H band and I bands get smaller.

The A band is named the “A band” because when first seen, they were anisotropic on light microscopy, and the I band is named the “I band” because they were isotropic on light microscopy. That isn’t helpful to anyone studying the sarcomere today. When Dustyn was studying, this is what he came up with to make it stick. It’s long, complicated, but it worked. If you can remember how they are named and which they are without this next section, great. If not, here’s how Dustyn did it.

The **A band** is the **alpha**, the “alpha and omega.” Being the alpha, A band is the biggest and strongest. And of course the biggest and baddest band would start in the middle and stretch his domain over everything he can. **A band** crosses the M line and represents the myosin AND myosin-actin overlap. The only thing free from the rule of A band are those loyal to Z line. The **I band** is the **light band** that crosses the **Z line** and reaches as far as it can, claiming whatever domain A band didn’t. Since the A band was myosin and myosin-actin, that leaves only actin-only for the I band. But there’s hope yet within A band’s kingdom. **H band** and **I band** grew up together (they are next to each other in the alphabet). H band is forming a revolution against A band. But the overlap group is too powerful (actin and myosin overlap delivers the powerstroke), so the only group H band can recruit is the myosin-only portion of A band’s forces. So both H band and I band are the light bands. I band is the actin-only that escaped A band’s tyranny, and H band is the myosin-only deep inside A band’s rule. The **H band** is the **light band** that crosses the **M line**.

VISUAL MEMORIZATION AND CHEATING	
Really dark line between two REALLY light patches	Z line and I band
Light line between long dark patches	M line and H band
The grey thing between the really light patches	A band

Table 11.1

Myofilaments

Now we'll discuss the thin myofilament, actin, and the thick myofilament, myosin, in more detail.

Actin is a **polymer** of globular actin (G-actin) that forms a long string of G-actins stuck together. This string of G-actins is called fibrous actin (F-actin). G-actin is the discrete unit; F-actin is the filament. But F-actin has another molecule twisting around it called **tropomyosin**. Tropomyosin, in its position, hides the myosin-binding site from myosin. The interaction of the **troponin** molecules and calcium is discussed in the next lesson.

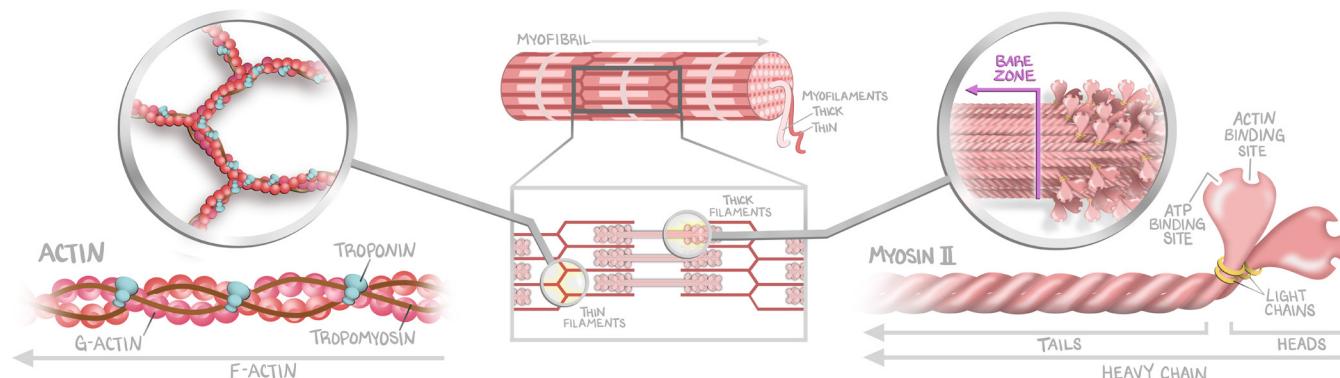


Figure 11.5: Actin and Myosin

This image shows the orientation and organization of the filaments. (Left side:) Thin filaments are made of actin. Discrete G-actin monomers string together to form the filamentous F-actin. F-actin is then encircled by tropomyosin. (Right side:) Thick filaments are made of myosin. Every myosin molecule consists of two light chains and two heavy chains. The heavy chains have two heads and two intertwined tails. (Magnifying glass, right:) The formation of the thick filament results in a myosin-head-free region called the bare zone, where the myosin heavy-chain tails are present without myosin heads.

The thick filaments are made of **myosin 2**, a dimer of **two heavy polypeptide chains** (each chain consisting of a head and a tail) associated with **four light chains** (like a necklace on the head of the heavy chain). A myosin 2 molecule has a tail of two interweaving tails, two lever arms, and two heads. When two of these myosin 2 molecules' tails meet, they team up, tail to tail, to create a double-sided **thick myosin filament**. They build tail to tail, heads on the edges. More and more myosin tails, staggered to the original heads, continue to add to the growing mass of myosin 2 molecules all wrapped up in each other. This is why the myosin filament is so thick, and why it's so dark on EM. Where there are no myosin heads, the original tail-to-tail connection is called the bare zone and is where the original two myosin filaments grab hold of the M line.

Contraction Changes the Length of Bands and the Position of Lines

When contraction occurs, myosin and actin slide past each other. The **Z lines get closer together**. The entire sarcomere gets shorter. EVERY sarcomere gets shorter all along the fibril. When contraction occurs, there will be **more actin and myosin overlap**. It should not be difficult to figure out what happens. The **M line** is still in the **Middle**. The **Z lines** get closer together. Since the actin is attached to them, the actin "goes deeper" towards the M line. That means the **I band** (the actin-free area) gets smaller. Likewise, since there's more overlap, the **H band** is smaller. The **A band doesn't change** because the M line didn't move, and the myosin didn't move, only the actin (review Figure 11.4).

Citations

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